

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

NO. 1:11-md-2242-RWZ

IN RE: PROGRAF ANTITRUST LITIGATION

ORDER

February 1, 2012

ZOBEL, D.J.

Plaintiffs, direct purchasers of prescription drugs, bring this one-count antitrust action under § 2 of the Sherman Act against Astellas Pharma US, Inc. (“Astellas”), a pharmaceutical manufacturer, and maker of Prograf, a branded prescription immunosuppressant used in organ transplant patients. Plaintiffs allege that defendant filed a baseless citizen petition with the Food and Drug Administration (“FDA”), with the sole intent of foreclosing market entry by generic competitors, that improperly extended its monopoly and kept Prograf prices at supra-competitive levels.

The United States Judicial Panel on Multidistrict Litigation transferred to this court, for pretrial purposes, five substantially identical cases pursuant to two orders (the “MDL”). Docket ## 1 and 2. Three additional cases filed in the District of Massachusetts have been associated with the MDL. Plaintiffs have filed a Consolidated Class Action Complaint (Docket # 11), which defendant moves to dismiss (Docket # 24).

I. The Complaint

The following descriptions and allegations derive entirely from the consolidated

complaint.

A. Drug Approval Process

Under the Federal Food, Drug and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301-392, manufacturers who create a new drug product must obtain approval of the FDA by filing a New Drug Application ("NDA"). An NDA must contain specific data concerning the safety and effectiveness of the drug.

In 1984, Congress passed the Hatch-Waxman Amendments that modified the FDCA by creating a streamlined process for bringing generic drugs to market without having to file lengthy and costly NDAs with the FDA. Under the new process, manufacturers of generic drugs may submit an Abbreviated New Drug Application ("ANDA"), which incorporates and relies on the scientific findings of safety and effectiveness established by the brand named drug's original NDA.

B. Prograf and Sandoz Inc.

Defendant manufactures, markets and sells "Prograf," a brand name prescription drug whose active ingredient is tacrolimus. Tacrolimus is an immunosuppressant used to prevent organ rejection by patients who have had liver, kidney or heart transplants. Prograf 1 mg and 5 mg capsules and injections were approved by the FDA in 1994, and 0.5mg capsules were approved in 1998.

On December 28, 2006, Sandoz Inc. filed an ANDA to market and sell generic tacrolimus capsules in 0.5, 1 mg, and 5 mg dosages.

C. Bioequivalence

To receive FDA approval, the prospective generic manufacturer must

demonstrate that the generic drug it seeks to market is "bioequivalent" to the brand name drug. Bioequivalence means that generic drug products must have the same "rate and extent of absorption" "when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions." Generic drugs proven to be bioequivalent to the branded drug, after laboratory testing, may be approved for sale under the ANDA procedure. The FDA publishes documents called "Guidance for the Industry" ("Guidance") to communicate to the public its current thinking on a subject, such as the appropriate method to determine bioequivalence. Guidance documents however, do not bind the FDA and serve only as recommendations.

In October 2000, the FDA published a Guidance on bioequivalence which articulated the FDA's then-current view that the proper tests to determine bioequivalence were single-dose studies conducted in healthy subjects representative of the general population.

In May 2007, the FDA published a Guidance on bioequivalence aimed at specific drugs. The Guidance specific for tacrolimus recommended that two clinical studies be conducted to demonstrate bioequivalence; one on healthy fasting subjects and the other on healthy fed subjects.

D. Citizen Petitions

Federal regulations allow individuals or entities to express concerns to the FDA about safety, scientific, or legal issues regarding a product anytime before, or after, its market entry by means of a citizen petition. Such a petition may request that the FDA take, or refrain from taking, any administrative action. 21 CFR § 10.30.

Plaintiffs allege that the FDA maintained a general unwritten policy, well known in the pharmaceutical industry, of considering and responding to relevant citizen petitions prior to approval of any related ANDA application because, as a practical matter, the FDA must first review the issues raised in a petition before it can evaluate its sufficiency.¹ The FDA's regulations provide a 180-day period for resolving citizen petitions. However, the complaint alleges that the FDA frequently takes much longer to respond.

On September 21, 2007, defendant filed a citizen petition with the FDA arguing primarily that bioequivalence testing for generic tacrolimus products should be conducted in actual transplant patients as well as healthy patients.

E. Astellas' Support for its Citizen Petition

In support of its citizen petition Astellas cited five clinical studies that compare branded and generic cyclosporine in transplant patients. Cyclosporine is another immunosuppressant drug used in transplant patients for which a generic formulation exists that Astellas asserted was analogous to Prograf for purposes of judging bioequivalence. While defendant acknowledged that three of the five studies showed no difference between branded and generic cyclosporine, it presented two studies that reported, what it considered to be, significant differences. Plaintiffs' dispute defendant's

¹ In 2007 Congress enacted the FDA Amendment Act of 2007, 21 U.S.C. § 355(q), which provides in relevant part that the FDA shall not delay approval of a pending ANDA because of a citizen petition unless the FDA determines that a delay is necessary to protect the public health. The amendments also provide that the FDA may summarily deny any citizen petition whose "primary purpose," as determined by the FDA, is to delay competition. The Act was signed into law on September 27, 2007, the FDA issued a Guidance noting the amendment would apply only to citizen petitions filed on or after September 27, 2009.

characterizations of the studies.

In Taber et al. (2005), researchers studied 88 patients prescribed generic cyclosporine and 100 patients prescribed branded cyclosporine after receiving a kidney transplant and concluded that six months post transplant, the patients who received the generic cyclosporine had a 14% higher proportion of acute rejection than those on the branded version.

In the Qazi et al. (2006) study, 73 kidney transplant patients who were converted from branded to generic cyclosporine and nine patients who remained on branded cyclosporine (the control group) were tracked. The authors reported that 18% of the patients in the generic group required a dose adjustment while no patients in the control group did.

As additional support Astellas cited reports from the National Kidney Foundation (1999) recommending that tacrolimus be studied further for demonstrating bioequivalence and that patients and physicians be educated on the risks associated with switching to a generic immunosuppressant. Astellas noted that the American Society of Transplantation published similar recommendations in 2003.

The petition also recounted Astellas' difficulties in demonstrating bioequivalence for an extended release form of tacrolimus, called Advagraf. According to Astellas, despite meeting the FDA's bioequivalence requirements in healthy volunteers, significant differences were observed in bioequivalence testing with kidney and liver transplant patients. Thus, Astellas suggested, bioequivalence of Advagraf to Prograf in healthy volunteers was not predictive of bioequivalence in transplant patients.

Synthesizing the data, defendant concluded that "[g]iven the potential deleterious effect in transplant patients and the consequences of losing a transplanted organ, FDA bioequivalence standards should require the evaluation of pharmacokinetics in transplant patients in the immediate post-transplant period."

F. Relief Requested by the Citizen Petition

As relief, the citizen petition requested that the FDA:

1. require all ANDA applicants for generic tacrolimus to demonstrate bioequivalence to innovator products by conducting studies in transplant patients in addition to healthy patients;
2. require warnings for all orally administered high risk immunosuppressant drugs used in transplant patients, which Astellas asserts includes tacrolimus, regarding the substitution of generic formulations for the brand name product;
3. add a section in the FDA "Orange Book" that highlights the risks of switching patients among different oral formulations of immunosuppressants, including tacrolimus; and
4. require generic manufacturers to distinguish their product from branded products (by use of different color/shape of capsule, container closure, packaging and source) and distinguish between dosage strengths.

G. The FDA's Response to the Citizen Petition

On August 10, 2009, nearly two years after Astellas filed its citizen petition, the FDA responded thereto in a detailed 15-page letter. It described numerous deficiencies in Astellas' submission and denied nearly all of the relief requested. It granted only Astellas' request that different dosages or strengths of generic tacrolimus be visibly differentiated from one another. On the same day, it also approved Sandoz' ANDA for generic tacrolimus.

H. Astellas' Post-Response Litigation

On August 11, 2009, one day after the FDA denied the citizen petition, Astellas sued the FDA in the District Court for the District of Columbia asserting that the decision was arbitrary and capricious and moved for a temporary restraining order seeking to stay the approval of the generic product. In its opposition FDA pointed out that "Sandoz's [ANDA] was pending for over [2 and ½] years. At least part of this period was directly attributable to the need to evaluate and respond to [Astellas' citizen petition]." The court accorded the FDA a high degree of deference in evaluating scientific data within its own area of expertise and denied the temporary restraining order.

Approximately one year and six months later, plaintiffs filed the instant complaint.

I. The Claims

The complaint alleges that U.S. Prograf sales were worth \$929 million for the 12 months ending in April 2009, and that the citizen petition was filed only for the purpose of extending Astellas' position as the sole tacrolimus provider, and not for any legitimate concern about the efficacy or safety of generic tacrolimus. Thus, defendant violated § 2 of the Sherman Act.

II. Defendant's Motion to Dismiss

Astellas moves to dismiss the consolidated complaint on the ground that its citizen petition was First Amendment activity entitled to Noerr-Pennington immunity. Eastern R.R. Presidents Conf. v. Noerr Motor Freight, Inc., 365 U.S. 127, 136-137 (1961); United Mine Workers of America v. James M. Pennington, 381 U.S. 657,

669-670 (1965). Docket # 24. Plaintiffs invoke the "sham exception" to such immunity which defendant says does not apply because it petitioned the FDA to act in its "quasi-legislative" and not in its adjudicatory capacity. Further, even if the sham exception were available, the complaint fails to allege facts sufficient to raise a plausible claim of its application. Lastly, Astellas contends that plaintiffs fail to sufficiently allege "cause-in-fact;" namely, that Astellas' citizen petition actually caused a delay in generic entry.

III. Standard

On a motion to dismiss, the "court takes as true all well-pleaded facts in the complaint[], scrutinize[s] them in the light most hospitable to the plaintiffs' theory of liability, and draw[s] all reasonable inferences therefrom in the plaintiffs' favor." Fothergill v. United States, 566 F.3d 248, 251 (1st Cir. 2009). The inquiry is limited to the facts alleged in the complaint, incorporated into the complaint, or susceptible to judicial notice. See In re Colonial Mortg. Bankers Corp., 324 F.3d 12, 15 (1st Cir. 2003). "To survive a motion to dismiss, a complaint must contain sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face.'" Ashcroft v. Iqbal, 129 S.Ct 1937, 1949 (2009). Plausibility "is not akin to a probability requirement, but [requires] more than a sheer possibility. . ." Id. "A pleading that offers 'labels and conclusions' or 'a formulaic recitation of the elements of a cause of action will not do.'" Id.

IV. Analysis

The Noerr-Pennington doctrine shields from liability under the antitrust laws

activities by individuals or groups designed to influence government policy or legislation. Noerr-Pennington immunity is similarly applicable to acts of advocacy before agencies and courts. California Motor Transport Co. v. Trucking Unlimited, 404 US 508, 510 (1972). However, when petitioning conduct is a "mere sham to cover what is actually nothing more than an attempt to interfere directly with the business relationship of a competitor" such conduct is not immune. Noerr, 365 U.S. at 144 (1961). The Supreme Court has established a two-pronged inquiry for determining whether the petitioning complained of is a "sham." Professional Real Estate Investors v. Columbia Pictures Industries, 508 U.S. 49, 61 (1993) ("PRE"). It may be considered a sham if it was (1) objectively baseless; and (2) subjectively a concealed attempt calculated to stifle competition. Id.

A. "Quasi-legislative" v. Adjudication Distinction

Before reaching the sufficiency of the complaint I address defendant's assertions that the Noerr-Pennington "sham" exception is not available when an antitrust defendant petitions an agency in its "quasi-legislative" capacity and not in its "adjudicatory capacity." Id. at 26-29. For this proposition, defendant relies principally on Kottle v. Northwest Kidney Centers, 146 F.3d 1056, 1061 (9th Cir. 1998).

In Kottle, the Ninth Circuit read a "legislative" versus "judicial" distinction into the traditional sham exception, holding that "the scope of the sham exception to the Noerr-Pennington doctrine depends on the branch of the government involved. If the forum is the legislature, the sham exception is extraordinarily narrow," but if the judiciary is implicated the sham exception is much broader. Id. at 1061-62, n.5. The

Kottle court reasoned that, in order to judge objective baselessness, courts need "objective standards, of which there are few, if any, in the political realm," and it cited language in California Motor Transport Co. that "fraud on a court cannot lightly be taken to apply in a legislative context ... the political arena has a higher tolerance for outright lies than the judicial arena does." Id. at 1061.

First, if the sham exception applied only to adjudicative processes, then any act of advocacy before a legislative or quasi-legislative body would be shrouded in carte blanche immunity regardless of purpose or sufficiency -- even if the activity was utterly baseless, an abuse of process, and motivated solely to stifle competition. Such a result is inconsistent with the reasoning underlying the doctrine espoused in Noerr and reiterated in subsequent Supreme Court cases. For example, PRE counsels that "Application of the Sherman Act [is] justified when petitioning activity ostensibly directed towards influencing governmental action, is a mere sham to cover ... an attempt to interfere directly with ... a competitor." PRE, 508 U.S. at 56.²

Second, defendant does not cite any authority that the Noerr-Pennington sham exception is categorically unavailable when agencies are petitioned in their "quasi-legislative" and not their "adjudicatory" capacity. Even Kottle did not go so far as to say that the sham doctrine would be completely inapplicable if the petitioning

² See also City of Columbia v. Omni Outdoor Advertising, Inc., 499 U.S. 365, 380-381 (1991) ("the sham exception to Noerr-Pennington encompasses situations in which persons use the governmental process -- as opposed to the outcome of that process -- as an anticompetitive weapon" for example where "delaying a competitor's entry into the market ... is sought [] by the lobbying process itself, and not by the governmental `action that the lobbying seeks"); California Motor Transport Co., 92 S. Ct. at 611-612 ("The right of petition ... Governs the approach of citizens or groups of them to administrative agencies" however, "First Amendment rights may not be used as a means or the pretext for achieving 'substantial evils.'").

implicated the state agencies' legislative capacity. Nor does defendant cite a single case alleging antitrust violations in connection with the filing of a citizen petition where the sham exception was found unavailable. To the contrary, at least one federal court has rejected the application of the Kottle distinction advocated by defendant specifically in the context of sham citizen petitions. See In re Flonase Antitrust Litigation v. Smithkline Beecham Corporation, 795 F. Supp. 2d 300, 310 n.11 (E. D. Pa. June 2, 2011).

For these reasons, I respectfully decline to follow Kottle. In any event, the FDA citizen petition process contains sufficient indicia of an adjudicatory proceeding to warrant application of the sham exception in this case.

Alternatively, defendant urges the court to determine as a matter of law that its citizen petition was a genuine attempt at advocacy designed to succeed on the merits. However, such a determination is only proper at this early stage when no facts are contested. PRE, 508 U.S. at 63. Where, as is the case here, the import and sufficiency of empirical findings and the consensus or lack thereof of the scientific community are hotly contested issues, such a finding as a matter of law is inappropriate. See In re Flonase, 795 F. Supp. 2d at 310 ("the question of whether a petition is a sham is generally a question of fact for the jury")(collecting cases). Cf. In re Gabapentin Patent Litigation, 649 F. Supp. 2d 340 (D. N.J. 2009); Hoffman-La Roche Inc. v. Genpharm Inc., 50 F. Supp. 2d 367, 380 (D. N.J. 1999); Scooter Store, Inc. v. Spinlife.com, LLC, 777 F. Supp. 2d 1102, 1115 (N. D. Ill. 2011).

B. Sufficiency of the Pleadings

The only issue to be determined now is the sufficiency of the plaintiffs' allegations in the complaint. See Jarrow Formulas, Inc. v. Int'l Nutrition Co., 175 F. Supp. 2d 296, 310-311 (D. Conn. 2001); In re Wellbutrin SR Antitrust Litigation, Nos. No. Civ.A. 04-5525, Civ.A. 04-5898, Civ.A. 05-396, 2006 WL 616292, at *6 - 7 (E. D. Pa. March 9, 2006).

As discussed, to survive a motion to dismiss plaintiffs must adequately plead that: (1) defendant's petitioning activity was "objectively baseless" in the sense that no reasonable petitioner before the agency "could realistically expect success on the merits;" and (2) that the baseless petitioning "concealed an attempt to interfere directly with the business relationship of a competitor through the use of the governmental process ... as an anti-competitive weapon." PRE, 508 U.S. at 61.

As to the first prong, the complaint states that: (1) the FDA found no merit to defendant's petition; (2) the materials provided by defendant failed to support its requested relief and, in particular, that the studies cited contained severe flaws in their methodology and design and reliance thereon was wholly unreasonable; (3) defendant "cherry picked" the information it presented, omitted disclosing limitations contained in the Taber study and misrepresented key information and conclusions from the other studies to mislead the FDA; and (4) the relief requested in the petition was unnecessary (and therefore baseless) because extensive monitoring of tacrolimus patients is already required and would have detected any issues related to switching from Prograf to the generic formulation.

On the second prong, plaintiffs allege in the complaint that: (1) defendant

advocated for relief in its citizen petition that it knew would not be granted by the FDA, and that had been previously and repeatedly rejected by the FDA; (2) Prograf sales were \$929 million for 2009, giving Astellas an incredibly strong financial incentive to extend its position as the sole tacrolimus provider; (3) the FDA maintained a practice, well known in the industry, that it would not approve generic ANDA petitions until it responded to and considered all related citizen petitions; (4) Astellas' citizen petition had the actual effect of delaying generic entry; and (5) Astellas purposely waited until the last possible moment to submit its citizen petition to the FDA before the law on citizen petitions changed to curb abuse, and months after the tacrolimus bioequivalence guidelines had been published.

These allegations are more than sufficient to withstand a motion to dismiss. See Skinder-Strauss Assos. v. Mass. Continuing Legal Educ., Inc., 870 F. Supp. 8, 10 (D. Mass. 1994).

C. Causation-in-Fact

Finally, defendant argues that plaintiffs have failed to plead "causation-in-fact" because they have not established that "but for Astellas' Citizen Petition, a generic tacrolimus product would have come to market," and contends that the complaint ignores an obvious alternative explanation that the review and collection of the FDA's solicited comments on the same subject, and not the citizen petition, may have caused the delay.

In their complaint, plaintiffs do allege that: (1) "on the same day the FDA [rejected the citizen petition it] also approved Sandoz's ANDA for generic tacrolimus

capsules;" (2) the FDA had "limited resources" and maintained a practice at the time of carefully considering "all citizen petitions" and responded in full to Astellas' citizen petition in a "detailed fifteen-page letter;" and (3) the FDA has stated, in public filings, that part of the 2 and a ½ year delay in approving Sandoz's ANDA petition was "directly attributable to the need to evaluate and respond' to Astellas' citizen petition."

This adequately and plausibly pleads causation.

V. Conclusion

For the foregoing reasons, defendant's motion to dismiss (Docket # 24) is
DENIED.

February 1, 2012

DATE

/s/Rya W. Zobel

RYA W. ZOBEL
UNITED STATES DISTRICT JUDGE